#### WHAT IS CLAIMED IS:

## 1. A compound of Formula I

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or a pharmaceutically acceptable salt thereof, wherein

R<sup>1</sup> is selected from the group consisting of:

10 (a) S(O)<sub>2</sub>CH<sub>3</sub>,

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- (b)  $S(O)_2NH_2$ ,
- (c)  $S(O)_2NHC(O)CF_3$ ,
- (d)  $S(O)(NH)CH_3$ ,
- (e)  $S(O)(NH)NH_2$ ,
- 15 (f)  $S(O)(NH)NHC(O)CF_3$ ,
  - (g) P(O)(CH<sub>3</sub>)OH, and
  - (h)  $P(O)(CH_3)NH_2$ ;

R<sup>2</sup> and R<sup>3</sup> each are independently selected from the group consisting of:

- (a) hydrogen,
- 20 (b) halo,
  - (c) C<sub>1-6</sub>alkoxy,
  - (d) C<sub>1-6</sub>alkylthio,
  - (e) CN,
  - (f) CF<sub>3</sub>,
- 25 (g) C<sub>1-6</sub>alkyl, and
  - (h) N3;

R4 is selected from the group consisting of

- (a) hydrogen,
- (b) C<sub>1-6</sub>alkyl, optionally substituted with 1-3 substituents independently selected from the group consisting of:
  - (i) halo,

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(ii) phenyl, naphthyl or HET<sup>1</sup>, each of said phenyl, naphthyl or HET<sup>1</sup> being optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C<sub>1</sub>-6alkyl, C<sub>1</sub>-6alkoxy, C<sub>1</sub>-6alkylthio, OH, CN, CF<sub>3</sub>, and CO<sub>2</sub>R<sup>6</sup>,

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- (iii) N(Ri)Rii, wherein Ri and Rii are each independently selected from the group consisting of hydrogen and C1-4alkyl,
- (iv) -CO<sub>2</sub>R<sup>iii</sup>, wherein R<sup>iii</sup> is hydrogen or C<sub>1-4</sub>alkyl,
- phenyl, naphthyl or HET<sup>2</sup>, each optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C<sub>1</sub>-6alkyl, C<sub>1</sub>-6alkoxy, C<sub>1</sub>-6alkylthio, OH, CN, CF<sub>3</sub>, and CO<sub>2</sub>R<sup>6</sup>;

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R<sup>5</sup> is selected from the group consisting of:

- (a)  $-NO_S$ ,
- (b)  $-C(O)-E-C_{1-10}$ alkyl-W-NO<sub>S</sub>,
- (c)

O  $(R^{a})_{0-3}$  —  $C-E-C_{0-6}$  alkyl —  $Ar-C_{0-6}$  alkyl —  $W-NO_{s}$ 

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wherein:

each s is independently 1 or 2,

E is a bond, oxygen, sulfur or -C(O)-O-,

each W is independently selected from the group consisting of:

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- (1) oxygen,
- (2) sulfur,
- (3)

$$CO_2R^b$$
 $-C CO_2R^b$ 

**(4)** 

$$\begin{array}{ccc}
O & CO_2R^b \\
-C-C-& \\
R^b
\end{array}$$

Ar is selected from the group consisting of: phenyl, naphthyl and HET3,

each Ra is independently selected from the group consisting of:

- 5 (1) halo,
  - (2) C<sub>1-6</sub>alkyl,
  - (3) C<sub>1-6</sub>alkoxy,
  - (4) C<sub>1-6</sub>alkylthio,
  - (5) OH,
- 10 (6) CN,
  - (7) CF<sub>3</sub>,
  - (8)  $CO_2R^7$ , and
  - (9)  $C_{0-6}$ alkyl-W- $NO_{s}$ ;

each Rb is independently selected from the group consisting of:

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(1) C<sub>1-6</sub>alkyl, optionally substituted with 1-3 halo groups or optionally substituted with phenyl, naphthyl or HET<sup>4</sup>, each of said phenyl, naphthyl or HET<sup>4</sup> being optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkoxy, C<sub>1-6</sub>alkylthio, OH, CN, CF<sub>3</sub>, and CO<sub>2</sub>R<sup>8</sup>; and

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phenyl, naphthyl or HET<sup>5</sup>, each optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C<sub>1</sub>-6alkyl, C<sub>1</sub>-6alkoxy, C<sub>1</sub>-6alkylthio, OH, CN, CF<sub>3</sub>, and CO<sub>2</sub>R<sup>8</sup>;

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R6, R7 and R8 are each independently selected from the group consisting of

- (a) hydrogen,
- (b) C<sub>1-6</sub>alkyl; and

HET<sup>1</sup>, HET<sup>2</sup>, HET<sup>3</sup>, HET<sup>4</sup> and HET<sup>5</sup> are each independently selected from the group consisting of: benzimidazolyl, benzofuranyl, benzopyrazolyl, benzotriazolyl, benzothiophenyl, benzoxazolyl, carbazolyl, carbolinyl, cinnolinyl, furanyl, imidazolyl,

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indolinyl, indolyl, indolazinyl, indazolyl, isobenzofuranyl, isoindolyl, isoquinolyl, isothiazolyl, isoxazolyl, naphthyridinyl, oxadiazolyl, oxazolyl, pyrazinyl, pyrazolyl, pyridopyridinyl, pyridazinyl, pyridyl, pyrimidyl, pyrrolyl, quinazolinyl, quinolyl, quinoxalinyl, thiadiazolyl, thiazolyl, thienyl, triazolyl, azetidinyl, 1,4-dioxanyl,
hexahydroazepinyl, piperazinyl, piperidinyl, pyrrolidinyl, morpholinyl, thiomorpholinyl, dihydrobenzimidazolyl, dihydrobenzofuranyl, dihydrobenzothiophenyl, dihydrobenzoxazolyl, dihydrofuranyl, dihydroimidazolyl, dihydroindolyl, dihydroisooxazolyl, dihydroisothiazolyl, dihydrooxadiazolyl, dihydrooxazolyl, dihydropyrazinyl, dihydropyrazolyl, dihydropyridinyl, dihydropyrimidinyl, dihydropyrrolyl, dihydroquinolinyl, dihydrotetrazolyl, dihydrothiadiazolyl, dihydrothiazolyl, dihydrothienyl, dihydrotriazolyl, dihydrothiadiazolyl, dihydrothiazolyl, dihydrothienyl, and tetrahydrothienyl.

# 2. A compound according to Claim 1 of Formula I

or a pharmaceutically acceptable salt thereof, wherein

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R<sup>1</sup> is selected from the group consisting of:

- (a)  $S(O)_2CH_3$ ,
- (b)  $S(O)_2NH_2$ ,
- (c)  $S(O)_2NHC(O)CF_3$ ,
- 25 (d)  $S(O)(NH)CH_3$ ,
  - (e)  $S(O)(NH)NH_2$ ,
  - (f)  $S(O)(NH)NHC(O)CF_3$ ,
  - (g)  $P(O)(CH_3)OH$ , and
  - (h)  $P(O)(CH_3)NH_2$ ;

R<sup>2</sup> and R<sup>3</sup> each are independently selected from the group consisting of:

- (a) hydrogen,
- (b) halo,

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- (c) C<sub>1-6</sub>alkoxy,
- (d) C<sub>1-6</sub>alkylthio,
  - (e) CN,

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- (f) CF<sub>3</sub>,
- (g) C<sub>1-6</sub>alkyl, and
- (h) N3;
- 10 R<sup>4</sup> is selected from the group consisting of
  - (a) hydrogen,
  - (b) C<sub>1-6</sub>alkyl, optionally substituted with 1-3 halo groups or optionally substituted with phenyl, naphthyl or HET<sup>1</sup>, each of said phenyl, naphthyl or HET<sup>1</sup> being optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkoxy, C<sub>1-6</sub>alkylthio, OH, CN, CF<sub>3</sub>, and CO<sub>2</sub>R<sup>6</sup>;
  - phenyl, naphthyl or HET<sup>2</sup>, each optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C<sub>1</sub>-6alkyl, C<sub>1</sub>-6alkoxy, C<sub>1</sub>-6alkylthio, OH, CN, CF<sub>3</sub>, and CO<sub>2</sub>R<sup>6</sup>;

R<sup>5</sup> is selected from the group consisting of:

- (a)  $-NO_S$ ,
- (b)  $-C(O)-E-C_{1-10}$ alkyl-W-NO<sub>S</sub>,

(c)

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$$(R^a)_{0-3}$$
 —  $C-E-C_{0-6}$  alkyl —  $Ar-C_{0-6}$  alkyl —  $NO_s$ ,

wherein:

each s is independently 1 or 2,

E is a bond, oxygen, sulfur or -C(O)-O-,

each W is independently selected from the group consisting of:

(1) oxygen,

(2) sulfur,

**(3)** 

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$$CO_2R^b$$
 $-C CO_2R^b$ 

$$\begin{array}{c}
O \quad CO_2R^b \\
-C-C-C \\
R^b
\end{array}$$

Ar is selected from the group consisting of: phenyl, naphthyl and HET<sup>3</sup>,

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each Ra is independently selected from the group consisting of:

- (1) halo,
- (2)  $C_{1-6}$ alkyl,
- (3)  $C_{1-6}$ alkoxy,

10 (4) C<sub>1-6</sub>alkylthio,

- (5) OH,
- (6) CN,
- (7) CF<sub>3</sub>,
- (8)  $CO_2R^7$ , and

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(9)  $C_{0-6}$ alkyl-W- $NO_{s}$ ;

each Rb is independently selected from the group consisting of:

- (1) C<sub>1-6</sub>alkyl, optionally substituted with 1-3 halo groups or optionally substituted with phenyl, naphthyl or HET<sup>4</sup>, each of said phenyl, naphthyl or HET<sup>4</sup> being optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkoxy, C<sub>1-6</sub>alkylthio, OH, CN, CF<sub>3</sub>, and CO<sub>2</sub>R<sup>8</sup>; and
- phenyl, naphthyl or HET<sup>5</sup>, each optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkoxy, C<sub>1-6</sub>alkylthio, OH, CN, CF<sub>3</sub>, and CO<sub>2</sub>R<sup>8</sup>;

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R6, R7 and R8 are each independently selected from the group consisting of

(a) hydrogen,

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(b) C<sub>1-6</sub>alkyl; and

HET<sup>1</sup>, HET<sup>2</sup>, HET<sup>3</sup>, HET<sup>4</sup> and HET<sup>5</sup> are each independently selected from the group consisting of: benzimidazolyl, benzofuranyl, benzopyrazolyl, benzotriazolyl, benzothiophenyl, benzoxazolyl, carbazolyl, carbolinyl, cinnolinyl, furanyl, imidazolyl, indolinyl, indolyl, indolazinyl, indazolyl, isobenzofuranyl, isoindolyl, isoquinolyl, isothiazolyl, isoxazolyl, naphthyridinyl, oxadiazolyl, oxazolyl, pyrazinyl, pyrazolyl, pyridopyridinyl, pyridazinyl, pyridyl, pyrimidyl, pyrrolyl, quinazolinyl, quinolyl, quinoxalinyl, thiadiazolyl, thiazolyl, thienyl, triazolyl, azetidinyl, 1,4-dioxanyl, hexahydroazepinyl, piperazinyl, piperidinyl, pyrrolidinyl, morpholinyl, thiomorpholinyl, dihydrobenzimidazolyl, dihydrobenzofuranyl, dihydrobenzothiophenyl, dihydrobenzoxazolyl, dihydrofuranyl, dihydroimidazolyl, dihydroimidazolyl, dihydrooxadiazolyl, dihydrooxazolyl, dihydropyrazinyl, dihydropyrazolyl, dihydropyridinyl, dihydropyrimidinyl, dihydropyriolinyl, dihydrothiadiazolyl, dihydrothiazolyl, dihydrothiazolyl, dihydrothiazolyl, dihydrothiazolyl, dihydrothiazolyl, dihydrothiazolyl, dihydrothiazolyl, dihydrothiazolyl, dihydrothiazolyl, dihydrothianyl, and tetrahydrothienyl.

## 3. The compound according to Claim 2 wherein

 $R^1$  is  $S(O)_2CH_3$ , and

R<sup>2</sup> and R<sup>3</sup> are both hydrogen.

4. The compound according to Claim 3 wherein:

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R<sup>4</sup> is C<sub>1-6</sub>alkyl, optionally substituted with 1-3 halo groups or optionally substituted with phenyl, naphthyl or HET<sup>1</sup>, each of said phenyl, naphthyl or HET<sup>1</sup> being optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkoxy, C<sub>1-6</sub>alkylthio, OH, CN, CF<sub>3</sub>, and CO<sub>2</sub>R<sup>6</sup>;

R6 is selected from the group consisting of

- (a) hydrogen,
- (b) C<sub>1-6</sub>alkyl; and

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HET1 is selected from the group consisting of: benzimidazolyl, benzofuranyl, benzopyrazolyl, benzotriazolyl, benzothiophenyl, benzoxazolyl, carbazolyl, carbolinyl, cinnolinyl, furanyl, imidazolyl, indolinyl, indolyl, indolazinyl, indazolyl, 5 isobenzofuranyl, isoindolyl, isoquinolyl, isothiazolyl, isoxazolyl, naphthyridinyl, oxadiazolyl, oxazolyl, pyrazinyl, pyrazolyl, pyridopyridinyl, pyridazinyl, pyridyl, pyrimidyl, pyrrolyl, quinazolinyl, quinolyl, quinoxalinyl, thiadiazolyl, thiazolyl, thienyl, triazolyl, azetidinyl, 1,4-dioxanyl, hexahydroazepinyl, piperazinyl, piperidinyl, pyrrolidinyl, morpholinyl, thiomorpholinyl, dihydrobenzimidazolyl, 10 dihydrobenzofuranyl, dihydrobenzothiophenyl, dihydrobenzoxazolyl, dihydrofuranyl, dihydroimidazolyl, dihydroindolyl, dihydroisooxazolyl, dihydroisothiazolyl, dihydrooxadiazolyl, dihydrooxazolyl, dihydropyrazinyl, dihydropyrazolyl, dihydropyridinyl, dihydropyrimidinyl, dihydropyrrolyl, dihydroquinolinyl, dihydrotetrazolyl, dihydrothiadiazolyl, dihydrothiazolyl, dihydrothienyl, dihydrotriazolyl, dihydroazetidinyl, methylenedioxybenzoyl, tetrahydrofuranyl, and 15 tetrahydrothienyl.

- 5. The compound according to Claim 4 wherein R<sup>4</sup> is methyl, ethyl, propyl or isopropyl.
  - 6. The compound according to Claim 3 wherein:

R<sup>4</sup> is phenyl, naphthyl or HET<sup>2</sup>, each optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkoxy, C<sub>1-6</sub>alkylthio, OH, CN, CF<sub>3</sub>, and CO<sub>2</sub>R<sup>6</sup>;

R6 is selected from the group consisting of

- (a) hydrogen,
- 30 (b) C<sub>1-6</sub>alkyl; and

HET<sup>2</sup> is selected from the group consisting of: benzimidazolyl, benzofuranyl, benzopyrazolyl, benzotriazolyl, benzothiophenyl, benzoxazolyl, carbazolyl, carbolinyl, cinnolinyl, furanyl, imidazolyl, indolinyl, indolyl, indolyl,

isobenzofuranyl, isoindolyl, isoquinolyl, isothiazolyl, isoxazolyl, naphthyridinyl, oxadiazolyl, oxazolyl, pyrazinyl, pyrazolyl, pyridopyridinyl, pyridazinyl, pyridyl, pyrimidyl, pyrrolyl, quinazolinyl, quinolyl, quinoxalinyl, thiadiazolyl, thiazolyl, thienyl, triazolyl, azetidinyl, 1,4-dioxanyl, hexahydroazepinyl, piperazinyl, piperazinyl, piperidinyl, pyrrolidinyl, morpholinyl, thiomorpholinyl, dihydrobenzimidazolyl, dihydrobenzofuranyl, dihydrobenzothiophenyl, dihydrobenzoxazolyl, dihydrofuranyl, dihydroimidazolyl, dihydroindolyl, dihydroisooxazolyl, dihydroisothiazolyl, dihydrooxadiazolyl, dihydrooxazolyl, dihydropyrazinyl, dihydropyrazolyl, dihydropyridinyl, dihydropyrimidinyl, dihydropyrrolyl, dihydroquinolinyl, dihydrotetrazolyl, dihydrothiadiazolyl, dihydrothiazolyl, dihydrothienyl, dihydrotriazolyl, dihydroazetidinyl, methylenedioxybenzoyl, tetrahydrofuranyl, and tetrahydrothienyl.

- 7. The compound according to Claim 3 wherein R<sup>5</sup> is -NO<sub>S</sub>,
- wherein s is 1 or 2.
  - 8. The compound according to Claim 3 wherein  $R^5$  is -C(O)-E-C<sub>1-10</sub>alkyl-W-NO<sub>s</sub>, wherein:
- 20 s is 1 or 2,

E is a bond, oxygen, sulfur or -C(O)-O-, W is selected from the group consisting of:

- (1) oxygen,
- (2) sulfur,
- (3)  $\begin{array}{c} CO_2R^b \\ -C \\ CO_2R^b \end{array}$

$$\begin{array}{c}
O \quad CO_2R^b \\
-C-C-C\\
R^b
\end{array}$$

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each Rb is independently selected from the group consisting of:

(1) C<sub>1-6</sub>alkyl, optionally substituted with 1-3 halo groups or optionally substituted with phenyl, naphthyl or HET<sup>4</sup>, each of said phenyl, naphthyl or HET<sup>4</sup> being optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkoxy, C<sub>1-6</sub>alkylthio, OH, CN, CF<sub>3</sub>, and CO<sub>2</sub>R<sup>8</sup>; and

phenyl, naphthyl or HET<sup>5</sup>, each optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C<sub>1</sub>-6alkyl, C<sub>1</sub>-6alkoxy, C<sub>1</sub>-6alkylthio, OH, CN, CF<sub>3</sub>, and CO<sub>2</sub>R<sup>8</sup>;

R8 is selected from the group consisting of

- (a) hydrogen and
- (b) C<sub>1-6</sub>alkyl; and

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HET<sup>4</sup> and HET<sup>5</sup> are each independently selected from the group consisting of: benzimidazolyl, benzofuranyl, benzopyrazolyl, benzotriazolyl, benzothiophenyl, benzoxazolyl, carbazolyl, carbolinyl, cinnolinyl, furanyl, imidazolyl, indolinyl, indolyl, indolazinyl, indazolyl, isobenzofuranyl, isoindolyl, isoquinolyl, isothiazolyl, isoxazolyl, naphthyridinyl, oxadiazolyl, oxazolyl, pyrazinyl, pyrazolyl, pyridopyridinyl, pyridazinyl, pyridyl, pyrimidyl, pyrrolyl, quinazolinyl, quinolyl, quinoxalinyl, thiadiazolyl, thiazolyl, thienyl, triazolyl, azetidinyl, 1,4-dioxanyl, hexahydroazepinyl, piperazinyl, piperidinyl, pyrrolidinyl, morpholinyl, thiomorpholinyl, dihydrobenzimidazolyl, dihydrobenzofuranyl, dihydrobenzothiophenyl, dihydrobenzoxazolyl, dihydrofuranyl, dihydroimidazolyl, dihydroindolyl, dihydroisooxazolyl, dihydroisothiazolyl, dihydropyridinyl, dihydropyrimidinyl, dihydropyrazinyl, dihydroquinolinyl, dihydrotetrazolyl, dihydrothiadiazolyl, dihydrothiazolyl, dihydrothiapyl, dihydrotriazolyl, dihydrothiadiazolyl, dihydrothiapyl, dihydrot

9. The compound according to Claim 8 wherein:

E is a bond or oxygen;

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s is 2;

W is oxygen; and

- 5 R<sup>4</sup> is hydrogen, methyl, ethyl, propyl or isopropyl.
  - 10. The compound according to Claim 3 wherein R<sup>5</sup> is

$$\begin{array}{c} O \\ -C - E - C_{0-6} \text{alkyl} - \left( \begin{array}{c} (R^a)_{0-3} \\ -C - E - C_{0-6} \text{alkyl} - (R^a)_{0-3} \end{array} \right) \\ -C - E - C_{0-6} \text{alkyl} - \left( \begin{array}{c} (R^a)_{0-3} \\ -C - E - C_{0-6} \text{alkyl} - (R^a)_{0-3} \end{array} \right) \\ -C - E - C_{0-6} \text{alkyl} - \left( \begin{array}{c} (R^a)_{0-3} \\ -C - E - C_{0-6} \text{alkyl} - (R^a)_{0-3} \end{array} \right) \\ -C - E - C_{0-6} \text{alkyl} - \left( \begin{array}{c} (R^a)_{0-3} \\ -C - E - C_{0-6} \text{alkyl} - (R^a)_{0-3} \end{array} \right) \\ -C - E - C_{0-6} \text{alkyl} - \left( \begin{array}{c} (R^a)_{0-3} \\ -C - E - C_{0-6} \text{alkyl} - (R^a)_{0-3} \end{array} \right) \\ -C - E - C_{0-6} \text{alkyl} - \left( \begin{array}{c} (R^a)_{0-3} \\ -C - E - C_{0-6} \text{alkyl} - (R^a)_{0-3} \end{array} \right) \\ -C - E - C_{0-6} \text{alkyl} - \left( \begin{array}{c} (R^a)_{0-3} \\ -C - E - C_{0-6} \text{alkyl} - (R^a)_{0-3} \end{array} \right) \\ -C - E - C_{0-6} \text{alkyl} - (R^a)_{0-3} \\ -C - E - C_{0-6} \text{alkyl} - (R^a)_{0-3} \end{array} \right) \\ -C - E - C_{0-6} \text{alkyl} - (R^a)_{0-3} \\ -C - E - C_{0-6} \\ -C - E - C_{0-6$$

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wherein:

each s independently 1 or 2,

15 E is a bond, oxygen, sulfur or -C(O)-O-,

each W is independently selected from the group consisting of:

- (1) oxygen,
- (2) sulfur,

20 (3)

$$CO_2R^b$$
 $-C^1$ 
 $CO_2R^b$ 

 $\begin{array}{ccc}
O & CO_2R^{t} \\
-C-C & \\
R^{b}
\end{array}$ 

each Ra is independently selected from the group consisting of:

- 25 (1) halo,
  - (2)  $C_{1-6}$ alkyl,
  - (3)  $C_{1-6}$ alkoxy,
  - (4) C<sub>1-6</sub>alkylthio,

- (5) OH,
- (6) CN,
- (7) CF3,

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- (8)  $CO_2R^7$ , and
- (9)  $C_{0-6}$ alkyl-W-NO<sub>S</sub>;

each Rb is independently selected from the group consisting of:

- (1) C<sub>1-6</sub>alkyl, optionally substituted with 1-3 halo groups or optionally substituted with phenyl, naphthyl or HET<sup>4</sup>, each of said phenyl, naphthyl or HET<sup>4</sup> being optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkoxy, C<sub>1-6</sub>alkylthio, OH, CN, CF<sub>3</sub>, and CO<sub>2</sub>R<sup>8</sup>; and
- phenyl, naphthyl or HET<sup>5</sup>, each optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C1-6alkyl, C1-6alkoxy, C1-6alkylthio, OH, CN, CF3, and CO2R<sup>8</sup>;

R<sup>7</sup> and R<sup>8</sup> is selected from the group consisting of

- (a) hydrogen and
- 20 (b) C<sub>1-6</sub>alkyl; and

HET<sup>4</sup> and HET<sup>5</sup> are each independently selected from the group consisting of: benzimidazolyl, benzofuranyl, benzopyrazolyl, benzotriazolyl, benzothiophenyl, benzoxazolyl, carbazolyl, carbolinyl, cinnolinyl, furanyl, imidazolyl, indolinyl, indolyl, indolazinyl, indazolyl, isobenzofuranyl, isoindolyl, isoquinolyl, isothiazolyl, isoxazolyl, naphthyridinyl, oxadiazolyl, oxazolyl, pyrazinyl, pyrazolyl, pyridopyridinyl, pyridazinyl, pyridyl, pyrimidyl, pyrrolyl, quinazolinyl, quinolyl, quinoxalinyl, thiadiazolyl, thiazolyl, thienyl, triazolyl, azetidinyl, 1,4-dioxanyl, hexahydroazepinyl, piperazinyl, piperidinyl, pyrrolidinyl, morpholinyl, thiomorpholinyl, dihydrobenzimidazolyl, dihydrobenzofuranyl, dihydrobenzothiophenyl, dihydrobenzoxazolyl, dihydrofuranyl, dihydroixadiazolyl, dihydroixadiazolyl, dihydrooxadiazolyl, dihydrooxazolyl, dihydropyridinyl, dihydropyrimidinyl, dihyd

dihydrothiadiazolyl, dihydrothiazolyl, dihydrothienyl, dihydrotriazolyl, dihydroazetidinyl, methylenedioxybenzoyl, tetrahydrofuranyl, and tetrahydrothienyl.

#### 11. A compound according to Claim 2 of Formula II

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or a pharmaceutically acceptable salt thereof, wherein

R4 is selected from the group consisting of:

C<sub>1-6</sub>alkyl, optionally substituted with 1-3 halo groups or optionally substituted with phenyl, naphthyl or HET<sup>1</sup>, each of said phenyl, naphthyl or HET<sup>1</sup> being optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkoxy, C<sub>1-6</sub>alkylthio, OH, CN, CF<sub>3</sub>, and CO<sub>2</sub>R<sup>6</sup>;

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(b) phenyl, naphthyl or HET<sup>2</sup>, each optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkoxy, C<sub>1-6</sub>alkylthio, OH, CN, CF<sub>3</sub>, and CO<sub>2</sub>R<sup>6</sup>;

R6 is selected from the group consisting of

(a) hydrogen and

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(b) C<sub>1-6</sub>alkyl;

s is 1 or 2; and

HET<sup>1</sup> and HET<sup>2</sup> are each independently selected from the group consisting of: benzimidazolyl, benzofuranyl, benzopyrazolyl, benzotriazolyl, benzothiophenyl,

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benzoxazolyl, carbazolyl, carbolinyl, cinnolinyl, furanyl, imidazolyl, indolinyl, indolyl, indolazinyl, indazolyl, isobenzofuranyl, isoindolyl, isoquinolyl, isothiazolyl, isoxazolyl, naphthyridinyl, oxadiazolyl, oxazolyl, pyrazinyl, pyrazolyl, pyridopyridinyl, pyridazinyl, pyridyl, pyrimidyl, pyrrolyl, quinazolinyl, quinolyl, quinoxalinyl, thiadiazolyl, thiazolyl, thienyl, triazolyl, azetidinyl, 1,4-dioxanyl, hexahydroazepinyl, piperazinyl, piperidinyl, pyrrolidinyl, morpholinyl, thiomorpholinyl, dihydrobenzimidazolyl, dihydrobenzofuranyl, dihydrobenzothiophenyl, dihydrobenzoxazolyl, dihydrofuranyl, dihydroimidazolyl, dihydroindolyl, dihydroisooxazolyl, dihydroisothiazolyl, dihydropyridinyl, dihydropyrimidinyl, dihydropyrrolyl, dihydroquinolinyl, dihydrotetrazolyl, dihydrothiadiazolyl, dihydrothiazolyl, dihydrothianyl, dihydrothiazolyl, dihydrothianyl, dihydrothiany

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- 12. The compound according to Claim 11 wherein R<sup>4</sup> is methyl, ethyl, propyl or isopropyl.
  - 13. The compound according to Claim 11 wherein

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R<sup>4</sup> is phenyl or benzyl, wherein said phenyl and the phenyl portion of said benzyl are each optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C<sub>1</sub>-6alkyl, C<sub>1</sub>-6alkoxy, C<sub>1</sub>-6alkylthio, OH, CN, CF<sub>3</sub>, and CO<sub>2</sub>R<sup>6</sup>; and

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R6 is selected from the group consisting of

- (a) hydrogen and
- (b) C<sub>1-6</sub>alkyl.

- 14. The compound according to Claim 11 wherein s is 2.
- 15. A compound according to Claim 2 of Formula III

$$\begin{array}{c|c} CH_3SO_2 & W-NO_s \\ \hline \\ R^a \end{array}$$

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5 or a pharmaceutically acceptable salt thereof, wherein

R<sup>4</sup> is selected from the group consisting of:

- (a) C<sub>1-6</sub>alkyl, optionally substituted with 1-3 halo groups or optionally substituted with phenyl, naphthyl or HET<sup>1</sup>, each of said phenyl, naphthyl or HET<sup>1</sup> being optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkoxy, C<sub>1-6</sub>alkylthio, OH, CN, CF<sub>3</sub>, and CO<sub>2</sub>R<sup>6</sup>;
- (b) phenyl, naphthyl or HET<sup>2</sup>, each optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C1-6alkyl, C1-6alkoxy, C1-6alkylthio, OH, CN, CF3, and CO2R<sup>6</sup>;

R6 is selected from the group consisting of

- (a) hydrogen,
- (b) C<sub>1-6</sub>alkyl;

20 Ra is hydrogen or Co-6alkyl-W-NOs.

each s is independently 1 or 2,

each W is independently selected from the group consisting of:

25 (1) oxygen,

- (2) sulfur,
- (3)

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$$\begin{array}{c}
CO_{2}R^{b} \\
-C - \\
CO_{2}R^{b},\\
CO_{2}R^{b},\\
\end{array}$$
(4)
$$\begin{array}{c}
O \quad CO_{2}R^{b} \\
-C - C - \\
R^{b}
\end{array}$$

5 each Rb is independently selected from the group consisting of:

- C1-6alkyl, optionally substituted with 1-3 halo groups or optionally substituted with phenyl, naphthyl or HET<sup>4</sup>, each of said phenyl, naphthyl or HET<sup>4</sup> being optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C1-6alkyl, C1-6alkoxy, C1-6alkylthio, OH, CN, CF3, and CO2R<sup>8</sup>; and
- phenyl, naphthyl or HET<sup>5</sup>, each optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkoxy, C<sub>1-6</sub>alkylthio, OH, CN, CF<sub>3</sub>, and CO<sub>2</sub>R<sup>8</sup>;
- 15 R<sup>8</sup> is selected from the group consisting of
  - (a) hydrogen,
  - (b) C<sub>1-6</sub>alkyl; and

HET1, HET2, HET4 and HET5 are each independently selected from the group
consisting of: benzimidazolyl, benzofuranyl, benzopyrazolyl, benzotriazolyl,
benzothiophenyl, benzoxazolyl, carbazolyl, carbolinyl, cinnolinyl, furanyl, imidazolyl,
indolinyl, indolyl, indolazinyl, indazolyl, isobenzofuranyl, isoindolyl, isoquinolyl,
isothiazolyl, isoxazolyl, naphthyridinyl, oxadiazolyl, oxazolyl, pyrazinyl, pyrazolyl,
pyridopyridinyl, pyridazinyl, pyridyl, pyrimidyl, pyrrolyl, quinazolinyl, quinolyl,
quinoxalinyl, thiadiazolyl, thiazolyl, thienyl, triazolyl, azetidinyl, 1,4-dioxanyl,
hexahydroazepinyl, piperazinyl, piperidinyl, pyrrolidinyl, morpholinyl,
thiomorpholinyl, dihydrobenzimidazolyl, dihydrobenzofuranyl,
dihydrobenzothiophenyl, dihydrobenzoxazolyl, dihydrofuranyl, dihydroimidazolyl,
dihydroindolyl, dihydroisooxazolyl, dihydroisothiazolyl, dihydrooxadiazolyl,
dihydrooxazolyl, dihydropyrazinyl, dihydropyrazolyl, dihydropyridinyl,

dihydropyrimidinyl, dihydropyrrolyl, dihydroquinolinyl, dihydrotetrazolyl, dihydrothiadiazolyl, dihydrothiazolyl, dihydrothianyl, dihydrotriazolyl, dihydrothiazolyl, dihydroazetidinyl, methylenedioxybenzoyl, tetrahydrofuranyl, and tetrahydrothienyl.

- 16. The compound according to Claim 15 wherein R<sup>4</sup> is methyl, ethyl, propyl or isopropyl.
  - 17. The compound according to Claim 15 wherein
- 10 R<sup>4</sup> is phenyl or benzyl, wherein said phenyl and the phenyl portion of said benzyl are each optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C<sub>1</sub>-6alkyl, C<sub>1</sub>-6alkoxy, C<sub>1</sub>-6alkylthio, OH, CN, CF<sub>3</sub>, and CO<sub>2</sub>R<sup>6</sup>; and
- 15 R6 is selected from the group consisting of
  - (a) hydrogen and
  - (b) C<sub>1-6</sub>alkyl.

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- 18. The compound according to Claim 15 wherein s is 2 and W is oxygen.
  - 19. The compound according to Claim 15 wherein R<sup>a</sup> is -CH<sub>2</sub>-W-NO<sub>s</sub>.
- 25 20. A compound according to Claim 2 of Formula IV

$$\begin{array}{c} \text{NO}_s \\ \text{W} \\ \text{C}_{0\text{-6}} \text{alkyl} \\ \text{R}^a \\ \text{IV} \\ \end{array}$$

5 or a pharmaceutically acceptable salt thereof, wherein

R<sup>4</sup> is selected from the group consisting of:

- (a) C<sub>1-6</sub>alkyl, optionally substituted with 1-3 halo groups or optionally substituted with phenyl, naphthyl or HET<sup>1</sup>, each of said phenyl, naphthyl or HET<sup>1</sup> being optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkoxy, C<sub>1-6</sub>alkylthio, OH, CN, CF<sub>3</sub>, and CO<sub>2</sub>R<sup>6</sup>;
- (b) phenyl, naphthyl or HET<sup>2</sup>, each optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkoxy, C<sub>1-6</sub>alkylthio, OH, CN, CF<sub>3</sub>, and CO<sub>2</sub>R<sup>6</sup>;

R6 is selected from the group consisting of

- (a) hydrogen,
- (b) C<sub>1-6</sub>alkyl;
- 20 Ra is hydrogen or Co-6alkyl-W-NO<sub>S</sub>.

each s is independently 1 or 2;

each W is independently selected from the group consisting of:

25 (1) oxygen,

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(2) sulfur,

$$\begin{array}{c}
CO_2R^b \\
-C - \\
CO_2R^b
\end{array}$$

$$\begin{array}{ccc}
O & CO_2R^b \\
-C-C-C & \\
R^b
\end{array}$$

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each Rb is independently selected from the group consisting of:

- C<sub>1-6</sub>alkyl, optionally substituted with 1-3 halo groups or optionally substituted with phenyl, naphthyl or HET<sup>4</sup>, each of said phenyl, naphthyl or HET<sup>4</sup> being optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkoxy, C<sub>1-6</sub>alkylthio, OH, CN, CF<sub>3</sub>, and CO<sub>2</sub>R<sup>8</sup>; and
- phenyl, naphthyl or HET<sup>5</sup>, each optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkoxy, C<sub>1-6</sub>alkylthio, OH, CN, CF<sub>3</sub>, and CO<sub>2</sub>R<sup>8</sup>;

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R8 is selected from the group consisting of

- (a) hydrogen,
- (b) C<sub>1-6</sub>alkyl; and
- HET¹, HET², HET⁴ and HET⁵ are each independently selected from the group consisting of: benzimidazolyl, benzofuranyl, benzopyrazolyl, benzotriazolyl, benzothiophenyl, benzoxazolyl, carbazolyl, carbolinyl, cinnolinyl, furanyl, imidazolyl, indolinyl, indolyl, indolazinyl, indazolyl, isobenzofuranyl, isoindolyl, isoquinolyl, isothiazolyl, isoxazolyl, naphthyridinyl, oxadiazolyl, oxazolyl, pyrazinyl, pyrazolyl, pyridopyridinyl, pyridazinyl, pyridyl, pyrimidyl, pyrrolyl, quinazolinyl, quinolyl, quinoxalinyl, thiadiazolyl, thiazolyl, thienyl, triazolyl, azetidinyl, 1,4-dioxanyl, hexahydroazepinyl, piperazinyl, piperidinyl, pyrrolidinyl, morpholinyl, thiomorpholinyl, dihydrobenzimidazolyl, dihydrobenzofuranyl, dihydroimidazolyl, dihydroimidazolyl, dihydroimidazolyl, dihydroimidazolyl, dihydroimidazolyl, dihydroixadiazolyl, dihydroixadiazolyl, dihydroixadiazolyl,

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dihydrooxazolyl, dihydropyrazinyl, dihydropyrazolyl, dihydropyridinyl, dihydropyrimidinyl, dihydropyrrolyl, dihydroquinolinyl, dihydrotetrazolyl, dihydrothiadiazolyl, dihydrothianyl, dihydrotriazolyl, dihydrotriazolyl, dihydroazetidinyl, methylenedioxybenzoyl, tetrahydrofuranyl, and tetrahydrothienyl.

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## 21. The compound according to Claim 20 of Formula IVa

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or a pharmaceutically acceptable salt thereof, wherein

R<sup>4</sup> is selected from the group consisting of:

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(a) C<sub>1-6</sub>alkyl, optionally substituted with 1-3 halo groups or optionally substituted with phenyl, naphthyl or HET<sup>1</sup>, each of said phenyl, naphthyl or HET<sup>1</sup> being optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkoxy, C<sub>1-6</sub>alkylthio, OH, CN, CF<sub>3</sub>, and CO<sub>2</sub>R<sup>6</sup>;

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(b) phenyl, naphthyl or HET<sup>2</sup>, each optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C1-6alkyl, C1-6alkoxy, C1-6alkylthio, OH, CN, CF3, and CO2R<sup>6</sup>;

R6 is selected from the group consisting of

(a) hydrogen,

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(b) C<sub>1-6</sub>alkyl;

Ra is hydrogen or Co-6alkyl-W-NOs.

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each s is independently 1 or 2;

each W is independently selected from the group consisting of:

each Rb is independently selected from the group consisting of:

- **(1)** oxygen,
  - (2) sulfur,

(3)

$$CO_2R^b$$
 $-C^ CO_2R^b$ 

**(4)** 

$$-\overset{1}{C}-\overset{2}{C}$$

$$-\overset{1}{C}O_{2}R^{b},$$

$$\overset{O}{C}O_{2}R^{b}$$

$$-\overset{1}{C}-\overset{1}{C}-\overset{1}{C}$$

$$\overset{1}{R}^{b}$$

- C<sub>1-6</sub>alkyl, optionally substituted with 1-3 halo groups or optionally (1) substituted with phenyl, naphthyl or HET4, each of said phenyl, naphthyl or HET4 being optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C1-6alkyl, C<sub>1-6</sub>alkoxy, C<sub>1-6</sub>alkylthio, OH, CN, CF<sub>3</sub>, and CO<sub>2</sub>R<sup>8</sup>; and
- phenyl, naphthyl or HET<sup>5</sup>, each optionally substituted with 1-3 **(2)** substituents independently selected from the group consisting of: halo, C<sub>1</sub>-6alkyl, C<sub>1</sub>-6alkoxy, C<sub>1</sub>-6alkylthio, OH, CN, CF<sub>3</sub>, and CO<sub>2</sub>R<sup>8</sup>;

R<sup>8</sup> is selected from the group consisting of

- (a) hydrogen,
- (b) C<sub>1-6</sub>alkyl; and

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HET1, HET2, HET4 and HET5 are each independently selected from the group consisting of: benzimidazolyl, benzofuranyl, benzopyrazolyl, benzotriazolyl, benzothiophenyl, benzoxazolyl, carbazolyl, carbolinyl, cinnolinyl, furanyl, imidazolyl, indolinyl, indolyl, indolazinyl, indazolyl, isobenzofuranyl, isoindolyl, isoquinolyl, isothiazolyl, isoxazolyl, naphthyridinyl, oxadiazolyl, oxazolyl, pyrazinyl, pyrazolyl,

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pyridopyridinyl, pyridazinyl, pyridyl, pyrimidyl, pyrrolyl, quinazolinyl, quinolyl, quinoxalinyl, thiadiazolyl, thiazolyl, thienyl, triazolyl, azetidinyl, 1,4-dioxanyl, hexahydroazepinyl, piperazinyl, piperidinyl, pyrrolidinyl, morpholinyl, thiomorpholinyl, dihydrobenzimidazolyl, dihydrobenzofuranyl,

dihydrobenzothiophenyl, dihydrobenzoxazolyl, dihydrofuranyl, dihydroimidazolyl, dihydroindolyl, dihydroisooxazolyl, dihydroisothiazolyl, dihydrooxadiazolyl, dihydrooxazolyl, dihydropyrazinyl, dihydropyrazolyl, dihydropyridinyl, dihydropyrimidinyl, dihydropyrrolyl, dihydroquinolinyl, dihydrotetrazolyl, dihydrothiadiazolyl, dihydrothiazolyl, dihydrothienyl, dihydrotriazolyl, dihydrothiadiazolyl, dihydrothiazolyl, tetrahydrofuranyl, and tetrahydrothienyl.

22. The compound according to Claim 21 wherein R<sup>4</sup> is methyl, ethyl, propyl or isopropyl.

23. The compound according to Claim 21 wherein

R<sup>4</sup> is phenyl or benzyl, wherein said phenyl and the phenyl portion of said benzyl are each optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C<sub>1</sub>-6alkyl, C<sub>1</sub>-6alkoxy, C<sub>1</sub>-6alkylthio, OH, CN, CF<sub>3</sub>, and CO<sub>2</sub>R<sup>6</sup>; and

R6 is selected from the group consisting of

- (a) hydrogen and
- (b) C<sub>1-6</sub>alkyl.

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- 24. The compound according to Claim 21 wherein s is 2 and W is oxygen.
- 30 25. The compound according to Claim 21 wherein R<sup>a</sup> is -CH<sub>2</sub>-W-NO<sub>s</sub>.
  - 26. The compound according to Claim 1 wherein: R<sup>4</sup> is C<sub>1-6</sub>alkyl, mono-substituted with

- (i) N(Ri)Rii, wherein Ri and Rii are each independently selected from the group consisting of hydrogen and C1-4alkyl or
- (ii) -CO<sub>2</sub>Riii, wherein Riii is hydrogen or C<sub>1</sub>-4alkyl.

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27. A compound selected from the following group:

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or a pharmaceutically acceptable

salt thereof,

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OH O2NO

or a pharmaceutically acceptable salt

10 thereof,

O or a pharmaceutically acceptable salt

thereof,

or a pharmaceutically acceptable salt

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thereof,

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or a pharmaceutically acceptable

salt thereof, and

28. A method of treating an inflammatory disease susceptible to treatment with a non-steroidal anti-inflammatory agent comprising administering to a patient in need of such treatment of a non-toxic therapeutically effective amount of a compound according to Claim 1.

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- 29. The method according to Claim 28 wherein the patient is also at risk of a thrombotic cardiovascular event.
- 30. A method of treating cyclooxygenase mediated diseases
  advantageously treated by an active agent that selectively inhibits COX-2 in
  preference to COX-1 comprising administering to a patient in need of such treatment
  of a non-toxic therapeutically effective amount of a compound according to Claim 1.
- 31. The method according to Claim 30 wherein the patient is also at risk of a thrombotic cardiovascular event.
  - 32. A method for treating a chronic cyclooxygenase-2 mediated disease or condition and reducing the risk of a thrombotic cardiovascular event in a human patient in need of such treatment and at risk of a thrombotic cardiovascular event comprising orally concomitantly or sequentially administering to said patient a compound according to Claim 1 in an amount effective to treat the cyclooxygenase-2 mediated disease or condition and aspirin in an amount effective to reduce the risk of the thrombotic cardiovascular event.
- 25 33. The method according to Claim 32 wherein the compound is administered orally on a once daily basis.
  - 34. The method according to Claim 32 wherein the compound is administered orally on a twice daily basis.

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35. The method according to Claim 32 wherein the cyclooxygenase-2 selective mediated disease or condition is selected from the group consisting of: osteoarthritis, rheumatoid arthritis and chronic pain.

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36. The method according to Claim 32 wherein aspirin is administered at a dose of about 30 mg to about 1 g.

- 37. The method according to Claim 36 wherein aspirin is administered at a dose of about 80 to about 650 mg.
  - 38. The method according to Claim 37 wherein aspirin is administered at a dose of about 81 mg or about 325 mg.
  - 39. The method according to Claim 32 wherein aspirin is orally administered once daily.
- 40. A pharmaceutical composition comprising a compound of formula I according to any one of claims 1 to 27, or a pharmaceutically acceptable salt thereof, and aspirin in combination with a pharmaceutically acceptable carrier.
- 41. A pharmaceutical composition comprising a compound of formula I according to any one of claims 1 to 27, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.
  - 42. A compound of formula I according to any one of claims 1 to 27, or a pharmaceutically acceptable salt thereof, for use in medical therapy.
  - 43. A compound of formula I according to any one of claims 1 to 27, or a pharmaceutically acceptable salt thereof, for use in treating an inflammatory disease susceptible to treatment with a non-steroidal anti-inflammatory agent.

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44. Use of a compound of formula I according to any one of claims 1 to 27, or a pharmaceutically acceptable salt thereof, for use in the manufacture of a medicament for treating cyclooxygenase mediated diseases advantageously treated by selective inhibition of COX-2 in preference to COX-1